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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/700,879	11/20/2000	Tatsuya Tamura	TAMURA-5	4195

1444 7590 07/01/2004

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WASHINGTON, DC 20001-5303

EXAMINER

MAIER, LEIGH C

ART UNIT	PAPER NUMBER
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1623

DATE MAILED: 07/01/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

<p align="center"><b>Office Action Summary</b></p>	<b>Application No.</b> 09/700,879	<b>Applicant(s)</b> TAMURA ET AL.	
	<b>Examiner</b> Leigh C. Maier	<b>Art Unit</b> 1623	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
  - If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
  - If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
  - Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 15 April 2004.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1,3,5-12,17-19 and 22-25 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1,3,5-12,17-19 and 22-25 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
     Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
     Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |   |   |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)  | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date <u>April 15, 2004</u> . | 6) <input type="checkbox"/> Other: _____  |

## **DETAILED ACTION**

### ***Status of the Claims***

Claim 1 has been amended. Claims 20 and 21 have been canceled. Claims 1, 3, 5-12, 17-19, and 22-25 are pending. Any objection or rejection not specifically repeated has been withdrawn. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Applicant's arguments with respect to the pending claims have been considered but are moot in view of the new grounds of rejection.

### ***Claim Rejections - 35 USC § 112 – 2<sup>nd</sup> paragraph***

Claims 12, 17, 19, and 25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 12, 17, and 25 depend from canceled claims 20 or 21. The claims are thereby rendered vague and indefinite.

Claim 19 has been amended to recite "wherein the spacer between at least one therapeutic agent . . . and hyaluronic acid . . . is selected from a group consisting of an amide bond, an ether bond and a sulfide bond." A fair reading of this claim would appear to allow for no more of a spacer than a simple covalent bond. However, claim 1 has been previously amended to expressly require a spacer between the therapeutic agent and HA. Therefore it is not clear if the limitation of "spacer" is met by a simple covalent bond or if this claim intends that the recited bond is the

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one between HA and the spacer, between the spacer and the therapeutic agent, or something else. If it is the one between HA and the spacer, it is not clear what Applicant intends with a sulfide or ether bond between the carboxyl and the spacer. The claim is thus rendered vague and indefinite.

***Claim Rejections - 35 USC § 102***

Claims 1, 8, 11, 12, 19, 23, and 24 are rejected under 35 U.S.C. 102(b) as being anticipated by PRESTWICH et al (US 5,874,417).

The reference discloses conjugates comprising HA linked to anti-inflammatories (ibuprofen, hydrocortisone, sulindac, indomethacin) via a spacer, wherein the spacer is attached to an HA carboxyl. See examples 2, 3, and 12. Example 2 discloses the preparation of HA-spacer-ibuprofen comprising the purification by gel filtration using water as an eluant, thereby producing a pharmaceutical composition. The compounds are disclosed as having utility in the treatment of various forms of arthritis. See col 14, lines 38-45.

***Claim Rejections - 35 USC § 103***

Claims 1, 3, 5-12, 17-19, and 22-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over PRESTWICH et al (US 5,874,417) and GALLARDY et al (WO 92/09556).

The invention is as set forth in the previous Office action.

PRESTWICH teaches as set forth above. The reference does not specifically exemplify the administration of the disclosed compounds for the treatment of joint diseases. However, the reference expressly suggests the use of other non-exemplified agents with known utility for the treatment of arthritis. See col 14, lines 42-45.

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GALLARDY teaches as set forth in previous Office actions.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the PRESTWICH conjugates by substituting hydroxamic acid derivatives, including those discussed in previous Office actions, for the treatment of joint disorders. One of ordinary skill would reasonably expect success in making such a modification and administration to a patient in need thereof for said disorders. It would be within the scope of the artisan to optimize the wt% of the therapeutic agent through routine optimization.

Claims 1, 3, 5-12, 17-19, and 22-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over PRESTWICH et al (US 5,874,417) and GALLARDY et al (WO 92/09556) in further view of (1) BEMIS et al (US 6,147,080) or (2) WUNDERLICH et al (US 6,066,332).

The invention is as set forth in the previous Office action. Claim 18 recites the use of a COX-2 inhibitor, MMP inhibitor, or an antirheumatic agent.

PRESTWICH and GALLARDY teach as set forth above. The references do not teach the full scope of the therapeutic agents recited in claim 18.

BEMIS and WUNDERLICH teach as set forth in the previous Office action.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to add another agent having utility in the treatment of arthritis, such as the anti-inflammatories taught by BEMIS and/or WUNDERLICH for the combined effects. One of ordinary skill would reasonably expect success in making such a modification.

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Applicant's amendment necessitated the new grounds of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

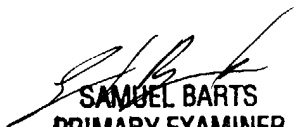
***Examiner's hours, phone & fax numbers***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leigh Maier whose telephone number is (571) 272-0656. The examiner can normally be reached on Tuesday, Wednesday, and Friday 7:00 to 3:30 (ET).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. James O. Wilson (571) 272-0661, may be contacted. The fax number for Group 1600, Art Unit 1623 is (703) 872-9306.

Visit the U.S. PTO's site on the World Wide Web at <http://www.uspto.gov>. This site contains lots of valuable information including the latest PTO fees, downloadable forms, basic search capabilities and much more.

Leigh C. Maier  
Patent Examiner  
June 23, 2004

  
**SAMUEL BARTS**  
**PRIMARY EXAMINER**  
**GROUP 1600**